UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,374	11/29/2001	Michael J. Heller	267/242	4021

34263 7590 11/22/2002

O'MELVENY & MEYERS
114 PACIFICA, SUITE 100
IRVINE, CA 92618

EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1637	9

DATE MAILED: 11/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/997,374	Applicant(s) HELLER, MICHAEL J.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Applicant has amended claim 1 to remove the monitoring step. This provides priority for this claim. However, claims 4, 12 and 13 retain either the monitoring limitation or a limitation of performing the step during PCR, neither limitation being taught in the parent applications. Therefore these claims are denied priority as discussed in the previous action. Therefore, claims 4, 12 and 13 of this application, while claiming priority to 08/250,951 will not be given such priority since the parent application lacks descriptive support for claim 4, 12 and 13. Consequently, the previous prior art rejection will be maintained with regard to these three claims.

2. Further, the examiner has reviewed the current specification itself, as well as the parent, U.S. Application 09/724,753, and finds that there is no descriptive support for the method of monitoring amplification other than that found in the claim itself. Since a claim can provide it's own written description, the originally filed claim is not new matter, but the current claim is not entitled to and will not be given priority to any of the parent applications because these applications do not provide descriptive support for the method of monitoring amplification.

Double Patenting

1. The obviousness type double patenting rejection is withdrawn in view of the terminal disclaimer.

Claim Rejections - 35 USC § 112

2. Claims 16-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, the last phrase "elongating of the target polynucleotide under conditions that the target polynucleotide sequence is amplifiable" is vague and indefinite. In particular, it is simply unclear how this phrase relates to the rest of the claim.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 4, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent 5,849,489) in view of Kidwell et al (U.S. Patent 5,332,659).

Heller teaches a method for detection of a target polynucleotide sequence (column 19), comprising the steps of:

providing a first polynucleotide sequence having one or more chromophores (column 19, lines 8-22);

providing a second polynucleotide sequence hybridized to the first polynucleotide sequence, the second polynucleotide sequence having one or more chromophores arranged in a quenching relationship to the acceptor chromophore of the first

polynucleotide sequence when the first polynucleotide sequence and second polynucleotide sequence are hybridized (column 19, lines 8-22);

exposing a target polynucleotide sequence to the hybridized first and second polynucleotide sequences (column 19, lines 26-30);

denaturing the hybridized first and second polynucleotide sequences (column 21, lines 20-31);

hybridizing the first polynucleotide sequence to the target polynucleotide sequence (column 19, lines 8-30);

hybridizing a third polynucleotide sequence having one or more donor chromophores to the target polynucleotide sequence (column 19, lines 8-30); and

irradiating the mixture to detect hybridization of the first polynucleotide sequence to the target polynucleotide sequence by fluorescence energy transfer from the one or more donor chromophores of the third polynucleotide sequence to the one or more acceptor chromophores of the first polynucleotide sequence (column 19, lines 31-40)

Heller further teaches wherein the target polynucleotide sequence comprises DNA RNA or synthetic polynucleotide (see column 21, lines 13-31).

Heller further teaches wherein the quenching chromophore is selected from the group consisting of 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid, 4-acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, 4-imethylaminophenylazophenyl-4-isothiocyanate (DABITC), Lucifer Yellow vinyl sulfone, Fluorescein isothiocyanate, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Rhodamine

X isothiocyanate, Texas Red (Sulforhodamine 101, sulfonyl chloride), Malachite Green isothiocyanate, or IR144. (see column 10, table 2).

Heller further teaches wherein the first polynucleotide sequence is bound to a solid support. (see claims 3-4).

Heller further teaches wherein the polynucleotide sequence comprises a plurality of donor chromophores. (see column 18).

Heller does not teach monitoring PCR amplification reactions.

Kidwell teaches monitoring of denatured and double stranded nucleic acids in PCR reactions in a homogeneous format during each PCR cycle (column 9, lines 1-19).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the method of Heller to monitor PCR reactions as taught by Kidwell since Kidwell states "A homogenous assay for polynucleic acid could be a valuable technique for the diagnosis of bacterial or viral infections" (column 9, lines 15-18). An ordinary practitioner would have been motivated to utilize the method of Heller to monitor PCR reactions in order to be able to diagnose in a rapid and efficient manner bacterial or viral infections.

4. Applicant has provided evidence in this file showing that the invention was owned by, or subject to an obligation of assignment to, the same entity at the time this invention was made. Accordingly, Heller et al (U.S. Patent 5,849,489) is disqualified as prior art through 35 U.S.C. 102(e), (f) or (g) in any rejection under 35 U.S.C. 103(a) in this application. However, this applied art additionally qualifies as prior art under another

subsection of 35 U.S.C. 102, specifically 35 U.S.C. 102(b), and accordingly is not disqualified as prior art under 35 U.S.C. 103(a).

4. Claims 1-3, 5-7, 10, 11, 14, 16-19, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cardullo et al (Proc. Natl. Acad. Sci. (1988) 85:8790-8794) in view of Morrison et al (Anal. Biochem. (1989) 183:231-244).

Cardullo teaches a method for detection of a nucleic acid sequence in a homogenous system in solution (page 8790, column 2) comprising the steps:

(a) providing a synthetic target nucleic acid sequence (see figure 1, panel B and page 8792, column 2, subheading "hybridization of two labeled ODNTs to a complementary strand"),

(b) providing a first polynucleotide sequence having at least one donor chromophore, fluorescein, which is complementary to a portion of the target nucleic acid sequence (see figure 1, panel B and page 8792, column 2, subheading "hybridization of two labeled ODNTs to a complementary strand"),

(c) providing a second polynucleotide sequence having at least one acceptor chromophore, Rhodamine, the second polynucleotide sequence being complementary to at least a portion of the target sequence (See figure 1, panel B and page 8792, column 2, subheading "hybridization of two labeled ODNTs to a complementary strand"),

(e) hybridizing the first and second polynucleotide sequences to the target nucleic acid sequence, such that when the first polynucleotide and second polynucleotide sequences are hybridized to the target nucleic acid sequence, the donor

chromophore and the acceptor chromophore are in an energy transfer relationship (see figure 1, panel B and page 8792, column 2, subheading "hybridization of two labeled ODNTs to a complementary strand"),

(f) irradiating the mixture to detect hybridization of the first and second polynucleotide sequences by fluorescence energy transfer from the donor chromophore to the acceptor chromophore (see figure 1, panel B, page 8791 and page 8792, column 2, subheading "hybridization of two labeled ODNTs to a complementary strand"),

Cardullo expressly discloses a situation comprising a plurality of donor or acceptor molecules (depending upon the fluorophore) noting "Finally, experiments were performed with the fluorescent dye acridine orange, which intercalates into double-helical nucleic acids and can act as either a donor or acceptor molecule to an appropriate fluorophore covalently attached to a hybridized ODNT (figure 1) (page 8790, column 2)."

Cardullo does not teach interposing a PCR amplification step prior to the detection energy transfer.

Morrison teaches amplification of double stranded DNA using PCR prior to detection of the double stranded DNA by fluorescence techniques (see page 240, subheading "Detection of amplified polynucleotides"). Morrison also teaches detection of RNA (page 243, column 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Cardullo to PCR amplify the target region before detection since Morrison notes "Therefore, the combination of the

hybridization sensitive probes and PCR amplification provided combined sensitivity, speed, specificity and simplicity (page 244, column 1)". An ordinary practitioner would have been motivated to combine PCR with the hybridization sensitive probes of Cardullo in order to improve sensitivity, specificity and speed as expressly taught by Morrison.

5. Claims 8, 9, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cardullo et al (Proc. Natl. Acad. Sci. (1988) 85:8790-8794) in view of Morrison et al (Anal. Biochem. (1989) 183:231-244) as applied to claims 1-3, 5-7, 14 and 16-19 and further in view of Matthews et al (Anal. Biochem. (1988) 169:1-25).

Cardullo in view of Morrison teach the limitations of claims 1-3, 5-7, 14 and 16-19 as discussed above. Cardullo in view of Morrison do not teach the use of solid support capture methods for detection.

Matthews teaches solid support immobilization strategies including the use of membranes (see page 15, table 7 and see page 14, subheading "solid supports" to page 16).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Cardullo in view of Morrison to use the solid supports of Matthews since Matthews notes that solid support methods are "simple and fairly rapid procedures (see page 14, column 2)" which are "well suited to the quantitation of specific nucleic acid sequences (see page 15, column 1)". An ordinary practitioner would have been motivated to use these standard techniques in order to detect the target nucleic acid using the method of Cardullo in view of Morrison

in order to simply and rapidly quantitate the amount of target nucleic acid present in a sample.

6. Claims 15 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cardullo et al (Proc. Natl. Acad. Sci. (1988) 85:8790-8794) in view of Morrison et al (Anal. Biochem. (1989) 183:231-244) as applied to claims 1-3, 5-7, 14 and 16-19 and further in view of Gelfand (U.S. Patent 5,322,770)

Cardullo in view of Morrison teach the limitations of claims 1-3, 5-7, 14 and 16-19 as discussed above. Cardullo in view of Morrison do not teach the use of RT-PCR to detect mRNA.

Gelfand teaches RT-PCR methods to amplify mRNA (see columns 3 and 4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Cardullo in view of Morrison to use the RT-PCR method of Gelfand since Gelfand notes "The present invention provides methods for the efficient amplification of RNA sequences requiring only one enzyme, a thermostable DNA polymerase. These methods offer simplicity and enhanced specificity over currently known methods (see column 2, lines 60-64)". An ordinary practitioner would have been motivated to use the RT-PCR technique of Gelfand in order to detect RNA target nucleic acid using the method of Cardullo in view of Morrison in order to simply and rapidly quantitate the amount of target nucleic acid present in a sample.

Response to Arguments

7. Applicant's arguments filed October 21, 2002 have been fully considered but they are not persuasive.

Applicant argues that the claim amendment overcomes the rejection of Heller in view of Kidwell. As noted above, this argument is found persuasive with regard to all the claims but claims 4, 12 and 13 which include limitations for which no basis in parent applications is found. With regard to the remaining claims, applicant's amendment necessitated the new grounds of rejection.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

November 20, 2002